

## REMARKS

### The Pending Claims

The pending claims are directed to a semiconductor particle complex comprising a semiconductor nanocrystal bound to a cationic polymer capable of enhancing the transport of the semiconductor nanocrystal across a biological membrane. Claims 1, 3-16 and 38-41 are pending and under active consideration. Claims 17-37 are withdrawn and claim 2 is canceled.

### The Office Action

Claims 1, 3-16 and 38-41 are rejected.

Claims 1, 3-7, 10-13, 16, 38, 39 and 41 are rejected under 35 U.S.C. 103(a), as being unpatentable over Bawendi et al. (U.S. Patent No. 6,306,610) in view of Rothbard et al. (U.S. Patent No. 6,306,993)

Claims 8, 9, 14, 15, and 40 are rejected under 35 U.S.C. 103(a), as being unpatentable over Bawendi et al. (U.S. Patent No. 6,306,610) in view of Frankel et al. (U.S. Patent No. 5,652,122).

### Amendments

No claims are currently amended.

**Summary of the Interview with the Examiner**

A telephone interview was conducted on October 4, 2006. Participating in the interview were Examiner Pensee T. Do of the United States Patent and Trademark Office, applicant's representatives, Joel Silver and Christopher Buntel, and Technical Area Manager for Invitrogen Nanosciences, Joseph Treadway. Discussed during the interview were the obviousness rejections to claims 1, 3-16 and 38-41.

Applicants contended that the current rejection based on Rothbard and Frankel combined with Bawendi was improper. Particularly, Applicants asserted that there was no motivation or reasonable expectation of success in combining the references, which individually and collectively taught away from the present claims. The Examiner agreed with applicant's contentions and requested that applicants submit a written response, which has been done in the following section of this paper.

Applicants would like to sincerely thank Examiner Do for her time and efforts in discussing the issues presented in the Official Action.

**Response to the Rejections**

I. Claims 1, 3-7, 10-13, 16, 38, 39 and 41 are rejected under 35 U.S.C. 103(a), as being unpatentable over Bawendi et al. (U.S. Patent No. 6,306,610) in view of Rothbard et al. (U.S. Patent No. 6,306,993). Applicants respectfully traverse this rejection.

Semiconductor nanocrystals are large rigid molecules made up of metals such as cadmium selenide and coated with, for example, a zinc sulfide shell, which can additionally be functionalized with charged molecules, such as fatty acids (Bawendi, Column 6, lines 18-50). Rothbard describes the transport of protein and small molecule compositions. Rothbard does not describe the transport of molecules resembling semiconductor nanocrystals. The only reference in Rothbard made to moieties having properties exhibited by semiconductor nanocrystals is in Column 8, lines 15-24: "attaching a large hydrophobic moiety may significantly impede or prevent cross-membrane transport due to adhesion of the hydrophobic moiety to the lipid bilayer."

In the current Office Action, the Examiner acknowledges that nanocrystals contain hydrophobic moieties, however, according to the Examiner, "large is the key word in Rothbard's statement. Nanocrystals may contain hydrophobic moieties, but not LARGE hydrophobic moieties." Applicants respectfully disagree. According to Rothbard, large hydrophobic moieties are molecules "such as lipid and fatty acid molecules." The hydrophobic portion of a semiconductor nanocrystal is vastly larger than a fatty acid or lipid molecule. In fact, nanocrystals can approach a mass of nearly 2,000 times that of a fatty acid. Accordingly, nanocrystals do contain "large" hydrophobic moieties.

Furthermore, the nanocrystals described in Bawendi are functionalized with fatty acids (see Figure 4), therefore Rothbard explicitly teaches away from the compositions in Bawendi by stating "the present invention includes conjugates that do not contain large hydrophobic moieties, such as lipid and fatty acid molecules." Rothbard at Column 8.

The current Office Action also alleges that statements made in the declaration pertaining to the characteristics of nanocrystals, particularly rigidity, hydrophobicity etc. are "nothing but an admission that the present invention is not enable [sic]." Page 6 of Office Action mailed July 11, 2006. As subsequently acknowledged by the Examiner in the interview on October 4, 2006, the claims are in fact enabled and the statements do not relate to enablement. Dr. Treadway's statements pertained to the difficulty confronted by a skilled artisan, such as himself, prior to the experimentation described in the present application. The fact that Applicants were able to successfully transport nanocrystals across biological membranes is indicia of enablement. As is overwhelmingly clear from the above discussion, prior to the present invention there was no teaching, suggestion, motivation or reasonable expectation of success identified in the references or the general common knowledge to arrive at the present claims. That is the point to be extracted from Dr. Treadway's statements.

"It is difficult but necessary that the decisionmaker forget what he or she has been taught . . . about the claimed invention and cast the mind back to the time the invention was made (often as here many years), to occupy the mind of one skilled in the art who is presented only with the references, and who is normally guided by the then-accepted wisdom in the art." *W.L. Gore &*

*Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303, 313 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984).

The Office Action also alleges that Dr. Treadway's statements are "irrelevant to the present invention because the invention claims nothing more than a semiconductor nanoparticle complex comprising a semiconductor nanocrystal bound to a cationic polymer, regardless of the purpose of which such combination is used for." Dr. Treadway's statements were directed to the lack of motivation, teaching away, and expectation of success in combining the references. The Examiner has repeatedly used the "purpose" of membrane transport as the reason for combining references. Accordingly, Dr. Treadway's statements are highly relevant to the current rejection.

The Office Action also asserts that "applicant's arguments are against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references." Applicants note that three criteria must be met to establish a *prima facie* case of obviousness: (1) there must be motivation to modify the reference or combine teachings; (2) there must be a reasonable expectation of success; and (3) the reference (or combination thereof) must teach or suggest all the claim limitations (emphasis added). Accordingly, for the purposes of establishing a *prima facie* case of obviousness, one cannot combine references without motivation and a reasonable expectation of success. Applicants have provided ample evidence to show that there is no motivation to combine the references, and in fact, they teach away from concomitant use.

In all, there simply is no motivation or reasonable expectation of success provided by the combination of Bawendi and Rothbard or Frankel to infer that a cationic polymer would improve transportability of a nanocrystal. Furthermore, the references in fact teach away from the use of the nanocrystals described in Bawendi. Accordingly, Applicants respectfully submit that the rejections over Bawendi in view of Rothbard under 35 U.S.C. §103(a) are improper and should be withdrawn.

II. Claims 8, 9, 14, 15, and 40 are rejected under 35 U.S.C. 103(a), as being unpatentable over Bawendi et al. (US 6,306,610) in view of Frankel et al. (US 5,652,122). Applicants respectfully traverse this rejection.

Claims 8, 9, 14, 15, and 40 are directed to a semiconductor particle complex comprising a semiconductor nanocrystal bound to an HIV tat peptide capable of enhancing the transport of the semiconductor nanocrystal across a biological membrane.

According to the present Office Action, "it would have been obvious to one of ordinary skills in the art to use the HIV tat peptide for transporting biological molecules across the cell membrane as taught by Frankel and attach it to a fluorescence semiconductor nanocrystal which associates to a cell membrane so that when biological molecules to be transported reach the cell membrane, they can be transported effectively and efficiently with the aid of the tat peptide and their activity or measurement can be detected by the nanocrystals since the nanocrystals have a spectral emission that is tunable to a desired wavelength, and wherein said wavelength provides information about a biological state or event." Applicants respectfully disagree.

Similar to Rothbard, the "cargo" molecules in Frankel are also biological molecules (i.e. peptides, nucleic acids, oligosaccharides). They inherently possess properties suited for biological systems, including hydrophilicity, flexibility, smaller size (as compared with nanocrystals) facile conjugation and limited ionic charges (as compared with nanocrystals).

On the other hand, nanocrystals, such as those described in Bawendi are large rigid molecules made up of metals such as cadmium selenide and coated with, for example, a zinc sulfide shell, which can additionally be functionalized with charged molecules, such as fatty acids. As with Rothbard, Frankel simply does not provide any motivation or reasonable expectation of success to arrive at a semiconductor particle complex comprising a semiconductor nanocrystal bound to an HIV tat peptide. Furthermore, the HIV tat moiety has been shown to be sequestered and inactivated by hydrophobic moieties, such as polystyrenesulfonate (PSS). See U.S. Patent No. 5,308,612.

Applicants have made it overwhelming clear that the semiconductor nanocrystals of the present invention simply do not conform to procedures described for transport of peptides, nucleic acids, oligosaccharides and the like. It is despite the teachings of Rothbard and Frankel that Applicants performed the experiments to arrive at the present invention showing enhanced delivery of nanocrystals through association with cationic polymers, not because of them.

### CONCLUSION

In view of the above remarks, it is submitted that this application is now ready for allowance. Early notice to this effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned agent at (541) 335-0165.

Respectfully submitted,

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/Joel Silver/

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